Citation:

Capel F, Viguerie N, Vega N, Dejean S, Arner P, Klimcakova E, Martinez JA, Saris WH, Holst C, Taylor M, Oppert JM, Sørensen TI, Clément K, Vidal H, Langin D. Contribution of energy restriction and macronutrient composition to changes in adipose tissue gene expression during dietary weight-loss programs in obese women. *J Clin Endocrinol Metab.* 2008 Nov;93(11):4315-22. Epub 2008 Sep 9.

PubMed ID: 18782868

Study Design:

Randomized Clinical Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to investigate the regulation of transcript levels according to calorie deficit and macronutrient composition (fat to carbohydrate ratio).

Inclusion Criteria:

Participants were female, obese and included if they were participants in the European multicenter Nutrient-Gene Interaction in Human Obesity (NUGENOB) study trial.

Exclusion Criteria:

Excluded if not included above.

Description of Study Protocol:

Recruitment

- Participants were recruited from a European multicenter Nutrient-Gene Interaction in Human Obesity (NUGENOB).

Design: Randomized clinical trial

- Participants were randomly assigned to one of two hypoenergetic diets (low-fat, high-carbohydrate diet (LF) or moderate-fat, low-carbohydrate (MF) diet).
- From 648 completers in the NUGENOB study, this study selected 94 participants (47 for each diet), matched for high quality of adipose tissue RNA, weight, height, body mass index

(BMI), waist-to-hip ratio, energy intake, macronutrient intake, and alcohol intake.

Blinding used (if applicable): implied with measurements

Intervention

- Participants were randomly assigned to one of two hypoenergetic diets (low-fat, high-carbohydrate diet (LF) or moderate-fat, low-carbohydrate (MF) diet) for 10 weeks.
- Both diets were designed to provide 600 calories less than the participant's estimated energy requirement.
- The LF diet was comprised of 20-25% of fat and 60-65% of carbohydrate.
- The MF diet was comprised of 40-45% fat and 40-45% carbohydrate.
- Both diets derived 15% of calories from protein.

Statistical Analysis

- Biological and anthropometric parameters were compared between sets and dietary groups using ANOVA. All changes were analyzed using paired-sample t-tests.

Data Collection Summary:

Timing of Measurements

Abdominal subcutaneous fat specimen (~1 gram) was obtained by needle aspiration before and after the dietary intervention.

Dependent Variables

- Abdominal subcutaneous fat specimen: About 1 gram was obtained by needle aspiration under local anesthesia after an overnight fast before and after the dietary intervention (biopsies were washed and stored in RNA Later preservative solution (QIAGEN, Courtaboeuf, France) at -80 degrees C until analysis.
- Total RNA: Extracted using the RNeasy total RNA minikit (QIAGEN) in the Inserm Toulouse laboratory (total RNA concentrations and integrity were estimated using Agilent 2100 bioanalyzer (Agilent Technologies, Massy, France).

Independent Variables

- Participants were randomly assigned to one of two hypoenergetic diets (low-fat, high-carbohydrate diet (LF) or moderate-fat, low-carbohydrate (MF) diet) for 10 weeks.
- Both diets were designed to provide 600 calories less than the participant's estimated energy requirement.
- The LF diet was comprised of 20-25% of fat and 60-65% of carbohydrate.
- The MF diet was comprised of 40-45% fat and 40-45% carbohydrate.
- Both diets derived 15% of calories from protein.

Control Variables

Description of Actual Data Sample:

Initial N: Original study had 648 completers. 94 selected (47 low-fat diet, 47 moderate-fat diet)

Attrition (final N): 94

Age: Not described

Ethnicity: Not described

Other relevant demographics: All participants were female and obese

Anthropometrics subjects were matched for anthropometric and biological parameters

Location: Multiple centers within Europe

Summary of Results:

Key Findings

- Averaged fat and carbohydrate intakes before the dietary interventions were similar between the low-fat (LF) and moderate-fat (MF) groups.
- The differences in fat or carbohydrate intakes between the two dietary groups were highly significant.
- Before the 10-week dietary intervention, LF and MF groups had similar BMI, fat-free mass, fat mass, waist-to-hip ratio, blood lipid and cholesterol profile, insulin levels and glucose levels.
- Energy restriction induced a similar and significant weight loss (-6.8 ± 0.2 kg), fat mass (-5.2 ± 0.2 kg), fat-free mass (-1.6 ± 0.2 kg) and BMI (-2.5 ± 0.1 kg/m^2) decrease in the two dietary groups.
- Changes induced by the diets were similar in the two groups (data not given).

Author Conclusion:

To conclude, during hypoenergetic diets, the primary determinant of changes in adipose tissue gene expression is energy restriction rather than the composition in fat and carbohydrate. The regulation in energy metabolism-related processes and co-regulatory pathways may explain the variations in anthropometric and biological parameters. However, the macronutrient content of the diets influences expression of a subset of genes, which may contribute to differential response in blood lipid profile.

Reviewer Comments:

Analysis completed on small subset of completers of a randomized clinical trial lasting only 10 weeks.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	No
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes